CLAIMS

1. A chip for assaying for a coronaviruse causing the severe acute respiratory syndrome (SARS-CoV) and a non-SARS-CoV infectious organism, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon an oligonucleotide probe complementary to a nucleotide sequence of SARS-CoV genome, said nucleotide sequence comprising at least 10 nucleotides, and one or more of the following oligonucleotide probe(s):

a) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism causing SARS-like symptoms, said nucleotide sequence comprising at least 10 nucleotides;

b) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV infectious organism damaging an infectious host's immune system, said nucleotide sequence comprising at least 10 nucleotides; or

c) an oligonucleotide probe complementary to a nucleotide sequence of a non-SARS-CoV coronaviridae virus, said nucleotide sequence comprising at least 10 nucleotides.

2. The chip of claim 1, which chip comprises a support suitable for use in nucleic acid hybridization having immobilized thereon at least two oligonucleotide probes complementary to at least two different nucleotide sequences of SARS-CoV genome, each of said two different nucleotide sequences comprising at least 10 nucleotides.

3. The chip of claim 2, wherein the at least two different nucleotide sequences of SARS-CoV genome comprises:

a) a nucleotide sequence of at least 10 nucleotides located within a conserved region of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a variable region of SARS-CoV genome; or

b) a nucleotide sequence of at least 10 nucleotides located within a structural protein coding gene of SARS-CoV genome and a nucleotide sequence of at least 10 nucleotides located within a non-structural protein coding gene of SARS-CoV genome.

4. The chip of claim 2, which further comprises:

a) at least one of the following three oligonucleotide probes: an immobilization control probe that is labeled and does not participate in any hybridization reaction when a sample containing or suspected of containing of a SARS-CoV or a non-SARS-CoV infectious organism is contacted with the chip, a positive control probe that is not complementary to any sequence of a SARS-CoV or non-SARS-CoV infectious organism but is complementary to a sequence contained in the sample not found in the SARS-CoV or the non-SARS-CoV infectious organism and a negative control probe that is not complementary to any nucleotide sequence contained in the sample; and

b) a blank spot.

5. The chip of claim 2, which comprises at least two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides, respectively, located within a conserved region of SARS-CoV genome, located within a structural protein coding gene of SARS-CoV genome or located within a non-structural protein coding gene of SARS-CoV genome.

6. The chip of claim 2, wherein:

a) the conserved region of SARS-CoV genome is a region located within the Replicase 1A or 1B gene or the Nucleocapsid (N) gene of SARS-CoV;

b) the structural protein coding gene of SARS-CoV genome is a gene encoding the Spike glycoprotein (S), the small envelope protein (E) or the Nucleocapsid protein (N); or

c) the non-structural protein coding gene of SARS-CoV genome is a gene encoding the Replicase 1A or 1B.

7. The chip of claim 2, wherein the variable region of SARS-CoV genome is a region located within the Spike glycoprotein (S) gene of SARS-CoV.

8. The chip of claim 2, which comprises at least two of the following four oligonucleotide probes: two oligonucleotide probes complementary to two different nucleotide sequences of at least 10 nucleotides located within the Replicase 1A or 1B gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence of at least 10 nucleotides located within the N gene of SARS-CoV and an oligonucleotide

probe complementary to a nucleotide sequence of at least 10 nucleotides located within the S gene of SARS-CoV.

9. The chip of claim 8, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a Replicase 1A or 1B nucleotide sequence, or a complementary strand thereof, that is set forth in Table 13; or

b) has at least 90% identity to a Replicase 1A or 1B nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 13.

10. The chip of claim 9, wherein one of the two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV comprises a nucleotide sequence that is set forth in Table 13.

11. The chip of claim 8, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a N nucleotide sequence, or a complementary strand thereof, that is set forth in Table 13; or

b) has at least 90% identity to a N nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 13.

12. The chip of claim 11, wherein the nucleotide sequence located within the N gene of SARS-CoV comprises a nucleotide sequence that is set forth in Table 13.

13. The chip of claim 8, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a S nucleotide sequence, or a complementary strand thereof, that is set forth in Table 13; or

b) has at least 90% identity to a S nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 13.

14. The chip of claim 13, wherein the nucleotide sequence located within the S gene of SARS-CoV comprises a nucleotide sequence that is set forth in Table 13.

15. The chip of claim 4, wherein the label of the immobilization control probe is selected from the group consisting of a chemical, an enzymatic, an immunogenic, a radioactive, a fluorescent, a luminescent and a FRET label.

16. The chip of claim 4, wherein the non-SARS-CoV-sequence is spiked in the sample to be assayed.

17. The chip of claim 16, wherein the spiked non-SARS-CoV-sequence is a sequence of *Arabidopsis* origin.

18. The chip of claim 8, which comprises two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV, an immobilization control probe that is labeled and does not participate in any hybridization reaction when a sample containing or suspected of containing of a SARS-CoV or a non-SARS-CoV infectious organism is contacted with the chip, a positive control probe that is not complementary to any sequence of a SARS-CoV or non-SARS-CoV infectious organism but is complementary to a sequence contained in the sample not found in the SARS-CoV or the non-SARS-CoV infectious organism and a negative control probe that is not complementary to any nucleotide sequence contained in the sample.

19. The chip of claim 18, which comprises multiple spots of the two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1B gene of SARS-CoV, the oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV, the oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV, the immobilization control probe, the positive control probe and the negative control probe.

20. The chip of claim 4, wherein at least one of the oligonucleotide probe comprises, at its 5' end, a poly dT region to enhance its immobilization on the support.

21. The chip of claim 2, wherein at least one of the oligonucleotide probes is complementary to a highly expressed nucleotide sequence of SARS-CoV genome.

22. The chip of claim 1, wherein the non-SARS-CoV infectious organism causing SARS-like symptoms is selected from the group consisting of a human coronaviruse 229E, a human coronaviruse OC43, a human enteric coronaviruse, an influenza virus, a parainfluenza virus, a respiratory sncytical virus, a human metapneumovirus, a rhinovirus, an adenoviruse, a mycoplasma pneumoniae, a chlamydia pneumoniae, a measles virus and a rubella virus.

23. The chip of claim 22, wherein the influenza virus is influenza virus A or influenza virus B.

24. The chip of claim 22, wherein the parainfluenza virus is selected from the group consisting of parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3 and parainfluenza virus 4.

25. The chip of claim 1, wherein the non-SARS-CoV infectious organism damaging an infectious host's immune system is selected from the group consisting of a hepatitis virus, a transfusion transmitting virus (TTV), a human immunodeficiency virus (HIV), a parvovirus, a human cytomegalovirus (HCMV), an Epstein-Barr virus (EBV) and a tre-ponema palidum.

26. The chip of claim 25, wherein the hepatitis virus is selected from the group consisting of hepatitis virus A (HAV), hepatitis virus B (HBV), hepatitis virus C (HCV), hepatitis virus D (HDV), hepatitis virus E (HEV) and hepatitis virus G (HGV).

27. The chip of claim 25, wherein the HIV is HIV I.

28. The chip of claim 25, wherein the parvovirus is parvovirus B19.

29. The chip of claim 1, wherein the non-SARS-CoV coronaviridae virus is selected from the group consisting of an avian infectious bronchitis virus, an avian infectious laryngotracheitis virus, a murine hepatitis virus, an equine coronaviruse, a canine coronaviruse, a feline coronaviruse, a porcine epidemic diarrhea virus, a porcine transmissible gastroenteritis virus, a bovine coronaviruse, a feline infectious peritonitis virus, a rat coronaviruse, a neonatal calf diarrhea coronaviruse, a porcine hemagglutinating encephalomyelitis virus, a puffinosis virus, a turkey coronaviruse and a sialodacryoadenitis virus of rat.

30. The chip of claim 1, wherein the support comprises a surface that is selected from the group consisting of a silicon, a plastic, a glass, a ceramic, a rubber, and a polymer surface.

31. A method for assaying for a SARS-CoV and a non-SARS-CoV infectious organism in a sample, which methods comprises:

a) providing a chip of claim 1;

b) contacting said chip with a sample containing or suspected of containing a nucleotide sequence of a SARS-CoV and a non-SARS-CoV infectious organism under conditions suitable for nucleic acid hybridization; and

c) assessing hybrids formed between said nucleotide sequence of said SARS-CoV or said non-SARS-CoV infectious organism, if present in said sample, and said oligonucleotide probe complementary to a nucleotide sequence of said SARS-CoV genome or said oligonucleotide probe complementary to a nucleotide sequence of said non-SARS-CoV infectious organism genome,

whereby detection of one or both of said hybrids indicates the presence of said SARS-CoV and/or said non-SARS-CoV infectious organism in said sample.

32. The method of claim 31, wherein the SARS-CoV is assayed by:

a) providing a chip of claim 2;

b) contacting said chip with a sample containing or suspected of containing a SARS-CoV nucleotide sequence under conditions suitable for nucleic acid hybridization; and

c) assessing hybrids formed between said SARS-CoV nucleotide sequence, if present in said sample, and said at least two oligonucleotide probes complementary to two different nucleotide sequences of SARS-CoV genome, respectively, to determine the presence, absence or amount of said SARS-CoV in said sample,

whereby detection of one or both said hybrids indicates the presence of said SARS-CoV in said sample.

33. The method of claim 31, wherein the SARS-CoV is assayed by:

a) providing a chip of claim 3;

b) contacting said chip with a sample containing or suspected of containing a SARS-CoV nucleotide sequence under conditions suitable for nucleic acid hybridization; and

c) assessing hybrids formed between said SARS-CoV nucleotide sequence, if present in said sample, and

i) said oligonucleotide probe complementary to a nucleotide sequence located within a conserved region of SARS-CoV genome and an oligonucleotide probe complementary to a nucleotide sequence located within a variable region of SARS-CoV genome, respectively; or

ii) said oligonucleotide probe complementary to a nucleotide sequence located within a structural protein coding gene of SARS-CoV genome and an oligonucleotide probe complementary to a nucleotide sequence located within a non-structural protein coding gene of SARS-CoV genome,

to determine the presence, absence or amount of said SARS-CoV in said sample, whereby detection of one or both said hybrids indicates the presence of said SARS-CoV in said sample.

34. The method of claim 31, wherein the SARS-CoV is assayed by:

a) providing a chip of claim 4;

b) contacting said chip with a sample containing or suspected of containing a SARS-CoV nucleotide sequence under conditions suitable for nucleic acid hybridization; and

c) assessing:

(i) hybrids formed between said SARS-CoV nucleotide sequence, if present in the sample, and the oligonucleotide probe complementary to a nucleotide sequence within a conserved region of SARS-CoV genome and an oligonucleotide probe complementary to a nucleotide sequence located within a variable region of SARS-CoV genome, respectively;

(ii) a label comprised in the immobilization control probe, or a hybrid(s) involving the positive control probe and/or the negative control probe; and

(iii) a signal at said blank spot

to determine the presence, absence or amount of said SARS-CoV in a sample.

35. The method of claim 34, wherein the chip comprises two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV, an oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV, an immobilization control probe, a positive control probe and a negative control probe and the presence of the SARS-CoV is determined when:

a) a positive hybridization signal is detected using at least one of the two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV, the oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV and/or the oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV;

b) a positive signal is detected from the immobilization control probe;

c) a positive hybridization signal is detected using the positive control probe;

d) a positive hybridization signal is not detected using the negative control probe; and

e) a positive hybridization signal is not detected at the blank spot.

36. The method of claim 35, wherein detecting a positive hybridization signal using at least one of the two oligonucleotide probes complementary to two different nucleotide sequences located within the Replicase 1A or 1B gene of SARS-CoV, or the oligonucleotide probe complementary to a nucleotide sequence located within the N gene of SARS-CoV, while not detecting a positive hybridization signal using the oligonucleotide probe complementary to a nucleotide sequence located within the S gene of SARS-CoV indicates mutation of the SARS-CoV.

37. The method of claim 31, wherein the chip of claim 21 is used and the method is used to diagnose early-stage SARS patients.

38. The method of claim 37, wherein the early-stage SARS patients have been infected with SARS-CoV from about less than one day to about three days.

39. The method of claim 31, which is used to determine whether a subject is infected by a SARS-CoV and/or a non-SARS-CoV infectious organism causing SARS-like symptoms.

40. The method of claim 39, wherein the SARS-like symptoms are caused by a non-SARS-CoV infectious organism selected from the group consisting of a human coronaviruse 229E, a human coronaviruse OC43, a human enteric coronaviruse, an influenza virus, a parainfluenza virus, a respiratory sncytical virus, a human metapneumovirus, a rhinovirus, an adenoviruse, a mycoplasma pneumoniae, a chlamydia pneumoniae, a measles virus and a rubella virus.

41. The method of claim 40, wherein the influenza virus is influenza virus A or influenza virus B.

42. The method of claim 40, wherein the parainfluenza virus is selected from the group consisting of parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3 and parainfluenza virus 4.

43. The method of claim 31, which is used to determine whether a subject is infected by a SARS-CoV and/or a non-SARS-CoV infectious organism damaging the subject's immune system.

44. The method of claim 43, wherein the non-SARS-CoV infectious organism damaging subject's immune system is selected from the group consisting of a hepatitis virus, a transfusion transmitting virus (TTV), a human immunodeficiency virus (HIV), a parvovirus, a human cytomegalovirus (HCMV), an Epstein-Barr virus (EBV) and a tre-ponema palidum.

45. The method of claim 44, wherein the hepatitis virus is selected from the group consisting of hepatitis virus A (HAV), hepatitis virus B (HBV), hepatitis virus C (HCV), hepatitis virus D (HDV), hepatitis virus E (HEV) and hepatitis virus G (HGV).

46. The method of claim 44, wherein the HIV is HIV I.

47. The method of claim 44, wherein the parvovirus is parvovirus B19.

48. The method of claim 31, which is used to determine whether a subject is infected by a SARS-CoV and/or a non-SARS-CoV coronaviridae virus.

49. The method of claim 48, wherein the non-SARS-CoV coronaviridae virus is selected from the group consisting of an avian infectious bronchitis virus, an avian infectious laryngotracheitis virus, a murine hepatitis virus, an equine coronaviruse, a canine coronaviruse, a feline coronaviruse, a porcine epidemic diarrhea virus, a porcine transmissible gastroenteritis virus, a bovine coronaviruse, a feline infectious peritonitis virus, a rat coronaviruse, a neonatal calf diarrhea coronaviruse, a porcine hemagglutinating encephalomyelitis virus, a puffinosis virus, a turkey coronaviruse and a sialodacryoadenitis virus of rat.

50. The method of claim 31, wherein the nucleotide sequence of the SARS-CoV or the non-SARS-CoV infectious organism is a genomic sequence of the SARS-CoV or the non-SARS-CoV infectious organism or a DNA sequence amplified from an extracted SARS-CoV RNA genomic sequence or an extracted genomic sequence of the non-SARS-CoV infectious organism.

51. The method of claim 50, wherein the SARS-CoV RNA genomic sequence is extracted from a SARS-CoV infected cell using the QIAamp Viral RNA kit, the Chomczynski-Sacchi technique or TRIzol.

52. The method of claim 50, wherein the SARS-CoV RNA genomic sequence is extracted from a SARS-CoV infected cell using the QIAamp Viral RNA kit.

53. The method of claim 31, wherein the genomic sequence of the of the SARS-CoV or the non-SARS-CoV infectious organism is extracted from a sputum or saliva sample, a lymphocyte of a blood sample.

54. The method of claim 31, wherein the genomic sequence of the of the SARS-CoV or the non-SARS-CoV infectious organism is extracted from nasopharyngeal, oropharyngeal, tracheal, bronchaleolar lavage, pleural fluid, urine, stool, conjunctiva, tissue from human, mouse, dog, rat, cat, horse, avian, earth, water, air.

55. The method of claim 50, wherein the genomic sequence of the of the SARS-CoV or the non-SARS-CoV infectious organism is amplified by PCR.

56. The method of claim 55, wherein a label is incorporated into the amplified DNA sequence during the PCR.

57. The method of claim 55, wherein the PCR comprises conventional, multiplex, nested PCR or RT-PCR.

58. The method of claim 55, wherein the PCR comprises a two-step nested PCR, the first step being a RT-PCR and the second step being a conventional PCR.

59. The method of claim 55, wherein the PCR comprises a one-step, multiplex RT-PCR using a plurality of 5' and 3' specific primers, each of the specific primers comprising a specific sequence complementary to its target sequence to be amplified and a common sequence, and a 5' and a 3' universal primer, the 5' universal primer being complementary to the common sequence of the 5' specific primers and the 3' universal primer being complementary to the common sequence of the 3' specific primers, and wherein in the PCR, the concentration of the 5' and 3' universal primers equals to or is higher than the concentration of the 5' and 3' specific primers, respectively.

60. The method of claim 59, wherein the 3' universal primer and/or the 5' universal primer is labeled.

61. The method of claim 60, wherein the label is a fluorescent label.

62. The method of claim 55, wherein the PCR comprises a multiplex nested PCR.

63. The method of claim 55, wherein the PCR is conducted using at least one of the following pairs of primers set forth in Table 18 or Tables 19-21.

64. An oligonucleotide primer for amplifying a nucleotide sequence of an influenza A virus, an influenza B virus, a human metapneumovirus, a human adenovirus, a human coronaviruse 229E or a human coronaviruse OC43, which oligonucleotide primer comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a target nucleotide sequence of influenza A virus, influenza B virus, human metapneumovirus, human adenovirus, human coronaviruse 229E or human coronaviruse OC43, or a complementary strand thereof, that is set forth in Tables 1-6; or

b) has at least 90% identity to a target nucleotide sequence of influenza A virus, influenza B virus, human metapneumovirus, human adenovirus, human coronaviruse

229E or human coronaviruse OC43 comprising a nucleotide sequence, or a complementary strand thereof, that is set forth in Tables 1-6.

65. The primer of claim 64, which comprises DNA, RNA, PNA or a derivative thereof.

66. The primer of claim 64, which comprises a nucleotide sequence, or a complementary strand thereof, that is set forth in Tables 1-6.

67. A kit for amplifying a nucleotide sequence of an influenza A virus, an influenza B virus, a human metapneumovirus, a human adenovirus, a human coronaviruse 229E or a human coronaviruse OC43, which kit comprises:

a) a primer of claim 64; and

b) a nucleic acid polymerase that can amplify a nucleotide sequence of an influenza A virus, an influenza B virus, a human metapneumovirus, a human adenovirus, a human coronaviruse 229E or a human coronaviruse OC43 using said primer of claim 64.

68. The kit of claim 67, wherein the nucleic acid polymerase is a reverse transcriptase.

69. An oligonucleotide probe for hybridizing to a nucleotide sequence of an influenza A virus, an influenza B virus, a human metapneumovirus, a human adenovirus, a human coronaviruse 229E or a human coronaviruse OC43, which oligonucleotide probe comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a target nucleotide sequence of influenza A virus, influenza B virus, human metapneumovirus, human adenovirus, human coronaviruse 229E or human coronaviruse OC43, or a complementary strand thereof, that is set forth in Tables 7-12; or

b) has at least 90% identity to a target nucleotide sequence of influenza A virus, influenza B virus, human metapneumovirus, human adenovirus, human coronaviruse 229E or human coronaviruse OC43, or a complementary strand thereof, that is set forth in Tables 7-12.

70. The probe of claim 69, which comprises DNA, RNA, PNA or a derivative thereof.

71. The probe of claim 69, which comprises a nucleotide sequence, or a complementary strand thereof, that is set forth in Tables 7-12.

72. The probe of claim 69, which is labeled.

73. The probe of claim 72, wherein the label is selected from the group consisting of a chemical, an enzymatic, an immunogenic, a radioactive, a fluorescent, a luminescent and a FRET label.

74. A kit for hybridization analysis of a nucleotide sequence of an influenza A virus, an influenza B virus, a human metapneumovirus, a human adenovirus, a human coronaviruse 229E or a human coronaviruse OC43, which kit comprises:

a) a probe of claim 69; and

b) a means for assessing a hybrid formed between a nucleotide sequence of an influenza A virus, an influenza B virus, a human metapneumovirus, a human adenovirus, a human coronaviruse 229E or a human coronaviruse OC43 and said probe.